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Successful Use of Grenz Rays for Disseminated Superficial Actinic Porokeratosis: Report of 8 Cases

Egle Ramelyte[a, b] Matilda Bylaite-Bucinskiene[b] Reinhard Dummer[a]
Laurence Imhof[a]

[a]Department of Dermatology, University Hospital Zurich, Zurich, Switzerland; [b]Vilnius University, Centre of Dermatovenereology, Vilnius, Lithuania

Keywords
Disseminated superficial actinic porokeratosis · Grenz rays · Radiotherapy

Abstract
Background: Disseminated superficial actinic porokeratosis (DSAP) is a rare keratinization disorder with potential malignant transformation, for which present treatment strategies show limited success. ***Aim:*** To evaluate the response of DSAP lesions to grenz ray radiotherapy (RTx). ***Methods:*** Data of patients treated with RTx at University Hospital Zurich, Switzerland, between 2004 and 2015, were reviewed. Patients with DSAP, who received at least 1 RTx treatment session and who had been followed up for at least 4 weeks were included in the further data analysis. ***Results:*** The study cohort consisted of 8 patients with a median age of 73 years (range 54–84). All were treated with grenz rays for DSAP. Most (7/8) patients showed complete clinical clearing of the lesions. All patients experienced temporary side effects of RTx, which resolved within 4 weeks after the last irradiation. ***Conclusion:*** We suggest radiotherapy with grenz rays as a treatment option for DSAP.

Introduction

Disseminated superficial actinic porokeratosis (DSAP) is the most common porokeratosis, first presenting in the 4th decade of life or later, and manifesting with widespread multiple small annular lesions on sun-exposed areas [1]. Histological presentation with a column of parakeratotic keratinocytes in a small epidermal invagination, also known as *cornoid lamella*, is considered a classical hallmark of all subtypes of porokeratosis. DSAP lesions are reported to have the potential of transformation into squamous cell carcinoma, Bowen's disease, or basal cell carcinoma [2] and usually cause cosmetic disturbances, therefore treatment is indicated. Various pharmacological and physical treatment options exist, but to our knowledge there is only 1 case report of successful porokeratosis treatment with grenz rays [3]. We present 8 cases of DSAP, successfully treated with radiotherapy (RTx) at the University Hospital Zurich.

Patients and Methods

For further details, see the supplementary material (for all online suppl. material, see www.karger.com/10.1159/000478855) (Fig. 1).

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Laurence Imhof, MD
Department of Dermatology, University Hospital of Zurich
Gloriastrasse 31
CH–8091 Zurich (Switzerland)
E-Mail laurence.imhof@usz.ch

Table 1. Clinical details of patients with DSAP

Pat.	Age, years/sex	Localization	Other skin pre-/ malignancies	Previous therapy	Total dose, Gy/RT type	Irradiated area, m^2/fields, *n*	Radio-dermatitis	FU, months/ relapse
1	81/F	Lower legs, forearms	AK, BCCs	Cryo, PDT	48/GR	0.0079/1	E3	26/no
2	73/M	Legs, arms, back	AKs, BCCs, SCC	Mometasone cream 1 mg/g, Cryo, PDT, imiquimod cream 5%	36/GR	0.094/4	E3	3/no
3	74/F	Legs and forearms	AKs, BCC	Cryo, ingenol mebutate 150 μg/g	29/GR	1.964/28	E3	46/clinically suspected
4	84/M	Lower legs, forearms	MB	–	32/GR	0.1931/5	E4	2/no
5	71/M	Lower legs, forearms	BCC, SCC, melanoma	Cryo, PDT, diclofenac gel 3%	52/GR	0.1713/4	E2	2/no
6	73/F	Forearms	Bowen's Ca, SCC	Tretinoin cream 0.05%	44/GR-SR	0.0824/7	E2	4.5/no
7	77/M	Legs	MB, AK	Adapalene cream, imiquimod cream 5%, Cryo	48/GR	at least 1.4995/25	E3	65/no
8	54/M	Lower legs	–	Acitretin 25 mg caps, PDT	30/SR-GR	was not measured/10	E5	24/no

Radiodermatitis: highest grade during treatment; FU, follow-up since the end of the first radiotherapy session; AK, actinic keratosis; BCC, basal cell carcinoma; Bowen's Ca, Bowen's carcinoma; Cryo, cryotherapy; GR, grenz rays; MB, Morbus Bowen; SCC, squamous cell carcinoma; SR, soft rays.

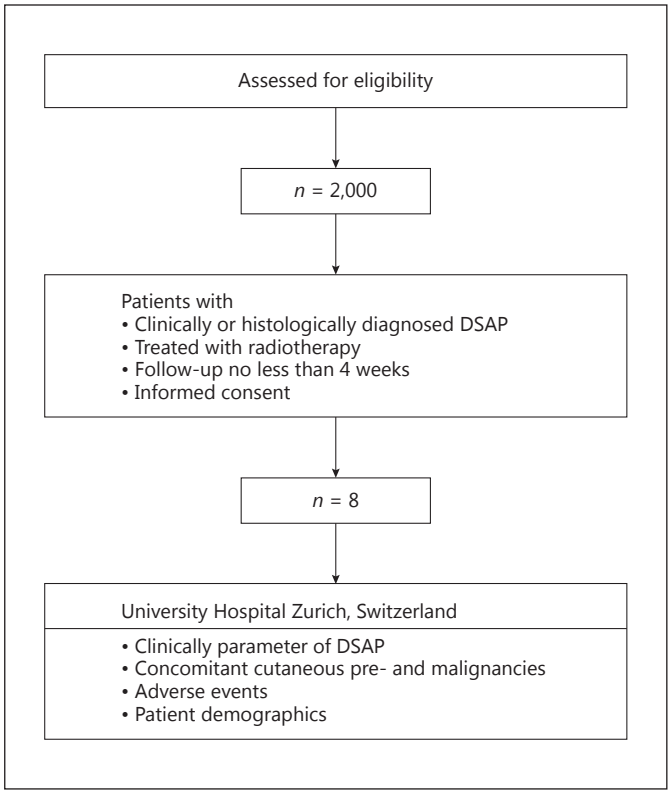

Fig. 1. Flowchart of Materials and Methods.

Results

The patient population included 5 men and 3 women, aged between 54 and 84 years (median 73). The patients had had the condition for at least 6 years prior to the first consultation at our clinic, and 7 out of 8 were pretreated with cryotherapy (5/7), photodynamic therapy (PDT) (5/7), topical steroids or other agents, such as imiquimod or ingenol mebutate. The used therapies showed only limited success, and all patients needed additional treatment.

Seven out of 8 patients had a history of actinic keratosis, while 6 out of 8 had been diagnosed with nonmelanoma skin cancer. The only patient who did not have a history of malignant skin lesions was also the youngest (54 years old). The distribution pattern of DSAP and cutaneous malignancies in the treatment population is shown in Figure 2.

All patients were treated with grenz rays (10 kV); 2 patients were additionally treated with soft rays (20 kV, 10–12 × 4 Gy) for Bowens' carcinoma and superficial squamous cell carcinoma. The total dose per field ranged from 28 to 52 Gy and was given at 3- to 4-day intervals for 6–10 sessions. In 1 case the therapy had to be discontinued after 6 sessions because of grade 5 acute reaction to RTx

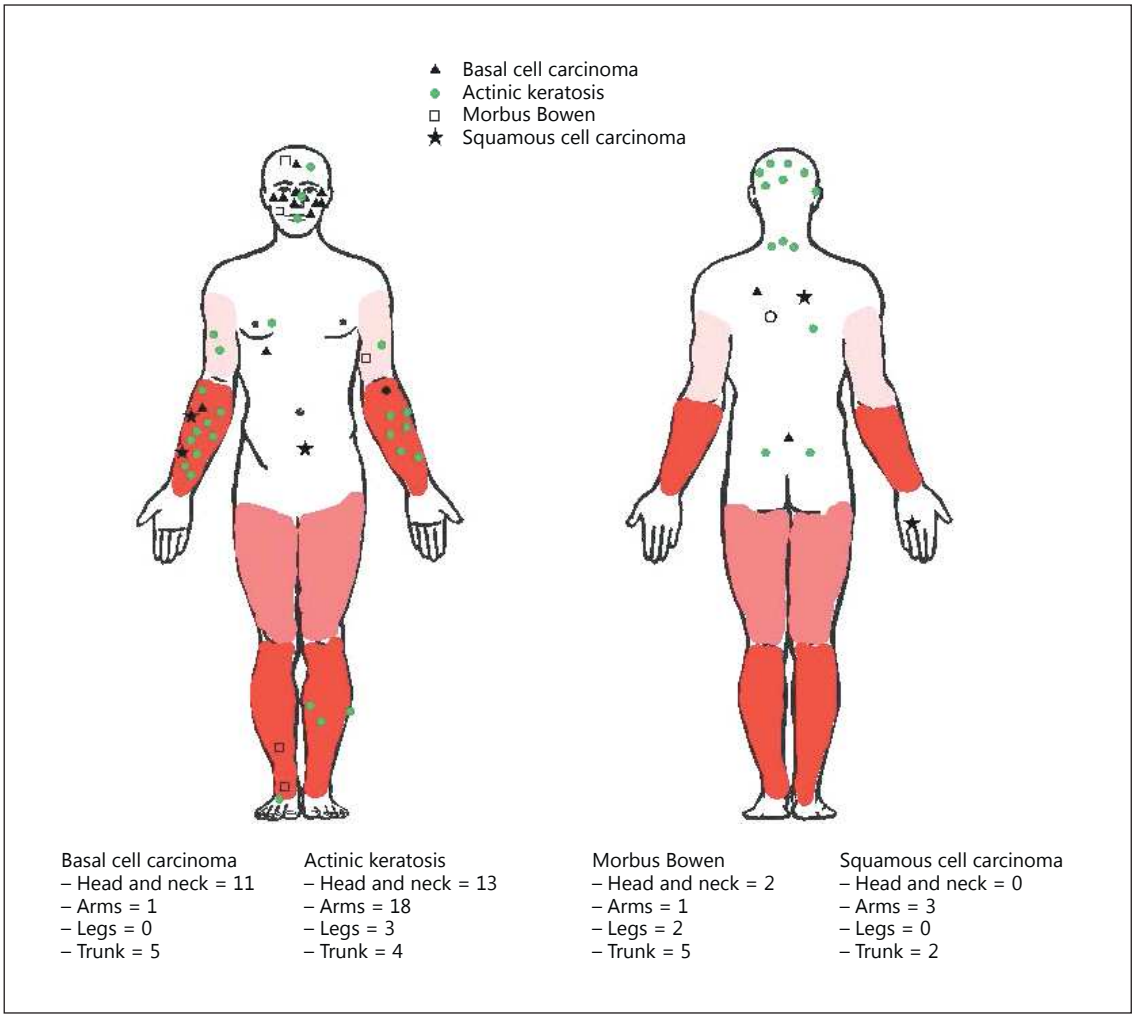

Fig. 2. Distribution of DSAP and concomitant cutaneous malignancies in the treatment population (cumulative view). Color intensity reflects presentation of lesions in marked area.

(patient 5). All patients were seen at least 4 weeks after RTx had ended and then were followed up for a median of 21.41 months (range 2–65 months).

At the time of the last follow-up, only 1 patient (patient 3) was clinically suspected to have 1 relapse lesion in the area, irradiated 4 years ago, but refused further investigation or treatment. No patients developed nonmelanoma skin cancer in the irradiated fields; however, 6 patients developed actinic keratosis or nonmelanoma skin cancer in other areas.

The patient characteristics are listed in Table 1; patient examples are provided in Figures 3 and 4.

Discussion

DSAP, although described more than 100 years ago, still lacks consistency in etiology and pathogenesis. Ultraviolet light, genetic factors (autosomal dominant inheritance, mutations in mevalonate kinase pathway) [4], immunosuppression, drugs, infections, and trauma [1] have all been reported to favor the development of DSAP. Irradiation with X-rays has been reported to provoke porokeratosis in 2 cases [5, 6]. Most hypotheses regarding the etiology state faulty maturation and early apoptosis rather than an increased rate of proliferation of keratinocytes being responsible for the formation of a cornoid lamella [4, 7]. Given the fact that all patients from our cohort de-

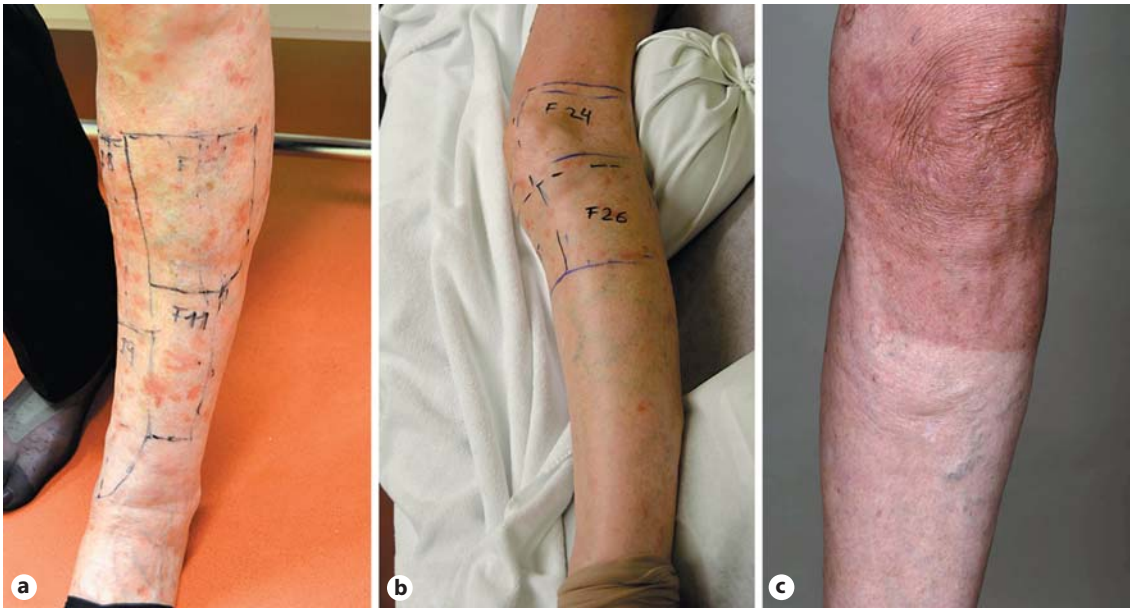

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Fig. 3. Patient No. 3: clinical presentation of DSAP and response to RTx. **a** DSAP lesions, distributed on lower legs and lower arms (not shown in the picture). **b** 15 months after RTx of left lower leg and marking for the therapy of the knee region. **c** 17 months after therapy on the lower leg and 2 months after therapy of the knee region shows clearing of the lesions.

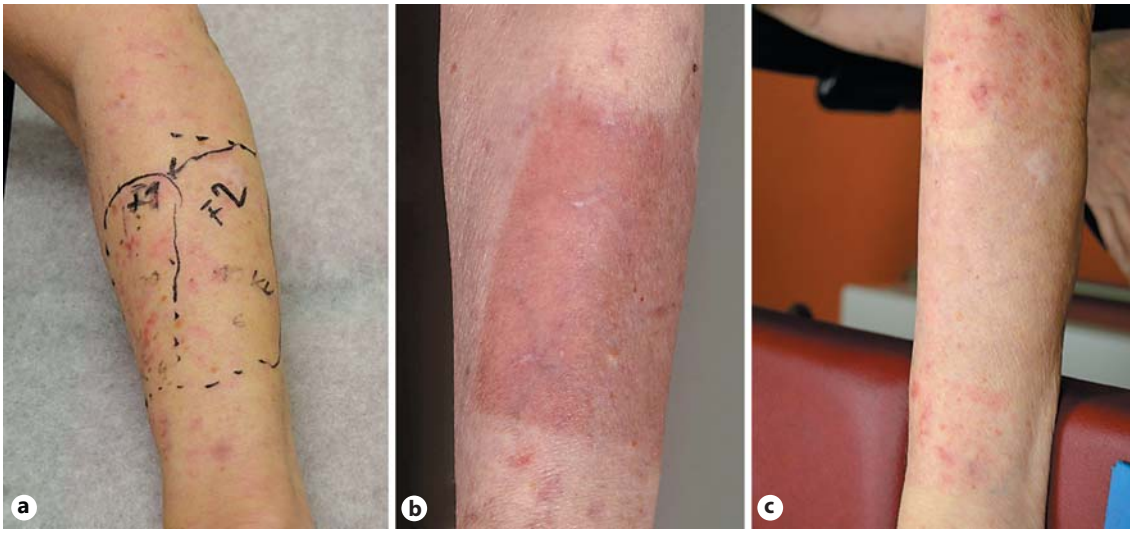

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Fig. 4. Patient No. 6: clinical presentation of DSAP and response to RTx. **a** Areas marked for RTx of DSAP and concomitant Bowen's carcinoma on the left forearm. **b** Grade 3 radiodermatitis after therapy with soft rays (20 kV, 4 Gy × 10 sessions, total 40 Gy) on the area with the carcinoma and with grenz rays (10 kV, 6 Gy × 8 sessions, total 48 Gy) on the area with actinic parakeratosis. **c** 2.5 months after therapy of the left forearm shows clearing of the lesions.

veloped DSAP on ultraviolet-exposed areas and the majority had pre- or malignant lesions in the same fields suggests defects in the DNA repair machinery as a possible trigger of the condition.

DSAP usually affects larger areas of the skin, which makes it difficult to treat with local therapies. Medications, used for the treatment of actinic keratosis, such as 5-fluorouracil, diclofenac gel 3%, imiquimod, retinoid and ingenol mebutate, or topical glucocorticoids could be suggested, but all show a limited effect [8]. In a retrospective study of Tan and Chong [9], a good response was achieved in only 15 and partial response in 53 of 94 patients, treated with various methods and for any type of porokeratosis. Larger areas of DSAP could be treated with PDT, but conventional PDT is a painful treatment option and shows conflicting results [10], whereas daylight PDT is a better tolerated option and has demonstrated a positive effect in 2 patients [11], but further investigations are needed.

Ultrasoft X-rays, used for RTx, are at the short-wavelength end of the electromagnetic spectrum (1 pm to 1 nm). RTx is known to cause DNA damage and cell death, mainly affecting rapidly dividing cells [12]. It has recently been reported to stimulate the expression of cancer-testis antigens and MHC-I molecules of tumor cells [13], as well as to cause local activation of complement [14] and increasing immune reaction in such a manner. Grenz rays have been reported to be a good treatment option for a number of inflammatory skin conditions [15]. Given the superficial location of pathology, low-energy radiation, such as grenz and soft rays (20 kV), that is absorbed within the first 2 mm of the skin [16], is suitable for the treatment of DSAP. The large field of irradiation as well as the possibility to adjust RTx to simultaneously treat malignancies, arising within DSAP, makes RTx an appealing therapy option. The recurrence rate after soft ray RTx was reported to be 13% in squamous cell carcinoma [17] and 15.8% in basal cell carcinoma [18]. Results from these studies along with an obvious clinical improvement noted in all of our patients with only 1 suspected relapse give a promising outlook for RTx as treatment option for DSAP. Nevertheless, larger clinical studies should be performed to provide more data regarding efficacy and safety.

Although an acute reaction to RTx is inevitable, it is usually mild in severity, transient and occurs only at the application site. It can be easily managed with black-tea dressings and hyaluronic acid cream, which makes RTx with grenz and soft rays a well-tolerable therapy.

Key Message

Radiotherapy with grenz rays could be a good treatment option for patients with disseminated superficial actinic porokeratosis.

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Statement of Ethics

Ethics approval for the collection of patient data and tissue samples was given by the Ethics Commission of Canton Zurich. Patient consent was obtained.

Disclosure Statement

No authors have any conflict of interest regarding this study.

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